

Remarks

Claims 1-61 are pending.

Rejections under 35 USC § 103

Curtet and Duclos.

Claims 1-61 are rejected under 35 USC § 103 as being obvious over Curtet (US Patent No. 4,895,726) in view of Duclos (US Patent 5,776,495).

Applicants respectfully traverse the rejection because Curtet does not disclose or suggest the claimed suspensions. At column 2, lines 5-20, Curtet states a process of:

- (i) mixing and co-micronizing fenofibrate and a solid surfactant;
- (ii) adding lactose and starch to the mixture; and converting the whole to granules in the presence of water;
- (iii) drying the granules until they contain no more than 1% water;
- (iv) grading the granules;
- (v) adding polyvinylpyrrolidone¹ and magnesium stearate to the graded granules; and
- (vi) filling gelatin capsules with the mixture.

Curtet states adding water to the mixture of fenofibrate and surfactant; drying the mixture; and subsequently adding polyvinylpyrrolidone.²

Curtet does not disclose or suggest any suspension of micronized fenofibrate. Additionally, Curtet never teaches a solution of at least one polymer, and does not provide any motivation to produce a solution containing at least one polymer. This is acknowledged by the PTO³ that:

"Curtet et al do not expressly state a fenofibrate suspension, but rather a composition [...]"

The PTO then continues and further states that:

¹ Curtet's working examples all use cross-linked polyvinylpyrrolidone.

² *Id.*

"Curtet et al do not expressly state a fenofibrate suspension, but rather a composition, wherein co-micronized granules are contained in the presence of water. However, it is well known in the art to incorporate a medicament, such as fenofibrate in combination with water and a surfactant to form a suspension."

The PTO contends that it is obvious for the skilled person to modify a solid composition into a liquid, aqueous, suspension comprising a surfactant. Claim 1, however, does not recite any surfactant (while claim 24 does).

Applicants respectfully submit that Curtet teaches away from a suspension. Indeed, Curtet states (e.g., abstract and claim 1):

"a composition containing a co-micronized mixture of particles of fenofibrate and a solid surfactant" (emphasis added).

Thus, Curtet requires the surfactant to be in a solid form. The claimed invention requires the surfactant or the polymer to be in a solution, hence, in a dissolved form, which is very different from a solid form. Accordingly, Curtet cannot render the claimed invention obvious.

Duclos does not cure the deficiencies of Curtet. Modifying Curtet to obtain a suspension, while Curtet requires a solid form, is not possible: the proposed modification (i.e., Duclos' solid dispersion) cannot change the principle of operation of Curtet's composition (i.e., containing a solid surfactant). See MPEP at 2143.02.

Duclos discloses and claims a process for preparing a solid dispersion (e.g., claim 1 and the abstract). Duclos states that a surfactant can assist in improving dissolution of poorly water-soluble drugs. Duclos provides the same statements as Curtet. Both references teach the use of a surfactant. However, Duclos discloses the use of surfactant in a solid dispersion. At page 2, lines 20-22, Duclos states that the process comprises the step of dissolving an active ingredient in an organic solvent (which may further contain the surfactant). This solution of active ingredient in a solvent with a polymer and a surfactant is then subjected to the process of forming the co-precipitate by using dissolution-evaporation (e.g., column 3, lines 1-2). The resulting composition is suitable for administering an active ingredient as a solid composition.

³ Office Action at page 5.

Duclos states that an intermediate solution can be used to produce the co-precipitate. A solution is distinct and different from a suspension.

The term "suspension" is well known in the art and is defined, for example, as follows:

(1): the state of a substance when its particles are mixed with but undissolved in a fluid or solid (2): a substance in this state (3): a system consisting of a solid dispersed in a solid, liquid, or gas usu. in particles of larger than colloidal size

Webster's New Collegiate Dictionary, G&C Merriam Company, page 1165 (1981).

The term "solution" is well known in the art and is defined, for example, as follows:

"solution (1) Dissolution. The mixing of a solid, liquid, or gaseous substance (solute) with a liquid (the solvent), forming a homogeneous mixture from which the dissolved substance can be recovered by physical processes. (2) The homogeneous mixture formed by the operation of s[olution]."

Grant & Hackh's Chemical Dictionary, 5th Ed., McGraw-Hill, Inc., page 541 (1987).

Because the terms solution and suspension are different, the solution of active ingredient of Duclos is different than the suspension of active ingredient of the claimed invention. Duclos does not teach a suspension of micronized active ingredient, but a solution containing the active ingredient in a dissolved form. The invention is, in contrast, directed to a suspension of fenofibrate in a micronized form.

The skilled person would not "*incorporate a suspension of micronized fenofibrate as taught by Duclos et al within the fenofibrate composition of Curtet et al*" as is stated by the PTO. Duclos fails to disclose a suspension. Water added in Curtet's process only serves granulation and will not allow a solution of surfactant to be produced. 8.9% of water based on the dry matter is used to granulate,⁴ excluding any solution of surfactant dissolved in water. Duclos teaches a process for the manufacture of a solid dosage form, using a solution of dissolved active ingredient.

Because none of the cited references discloses or teaches a suspension, the claimed invention cannot be obvious over the prior art.

⁴ See Curtet at Preparations 1-4.

Contrary to what the PTO states: "*because Duclos teach micronization of medicaments in suitable form such as suspensions, can be beneficial in increasing the solubility of active components and thereby improving the kinetics of resorption and consequently, the bioavailability of active ingredients,*" Duclos does not teach micronization. Duclos is only concerned with micronization at column 1, lines 24-37, in the section dedicated to the prior art. First, this statement is a very broad statement, and not based on references. Second, Duclos immediately criticized these existing possibilities. Thus, Duclos teaches away from using micronized active ingredient (with or without a surfactant). Duclos provides a technical approach which involves a dissolution step, whereby the micronization is necessarily lost (and is not recovered during the later stages of the process, including evaporation).

The claimed invention provides a suspension of an active ingredient, which is an intermediate product which is used in the manufacture of a final composition which exhibits superior results. *See* Specification at page 7, lines 19-21. The specific suspension, when used in a fluidized bed granulator, provides a final composition having an improved dissolution. The suspension itself is not used as a dosage form for the active ingredient, but as an intermediate in the manufacture of the final dosage form. Hence, it is irrelevant whether micronized fenofibrate in a suspension would provide increased bioavailability, because the suspension is not administered to a patient. Only the solid dosage form obtained from said suspension is administered to a patient, where the dosage form thus obtained exhibits an improved dissolution profile and consequently an improved bioavailability.

In view thereof, Applicants respectfully submit that the claimed invention is unobvious over Curtet in view of Duclos, and respectfully request that the rejection under 35 USC § 103 be withdrawn.

Curtet and Ikeda.

Claims 1-61 are rejected under 35 USC § 103 as being obvious over Curtet (US Patent No. 4,895,726) in view of Ikeda (US Patent 5,952,356).

Curtet has been analyzed above, the analysis of which is incorporated by reference herein in its entirety.

Ikeda does not cure the deficiencies of Curtet. Ikeda is directed to a specific combination of an antidiabetic, comprised of an insulin sensitivity enhancer, together with another antidiabetic having a different mode of action. Ikeda identifies eight other categories of drugs that have a different mode of action, including fibrates.⁵ Ikeda then identifies fifteen different fibrate compounds, one of which is fenofibrate.⁶ Ikeda states no preference for any fibrate compound. Ikeda does not provide any working or prophetic examples that use any type of fibrate or any of the fifteen different fibrate compounds identified therein. Ikeda is also completely alien to the issue of increasing the bioavailability of fenofibrate. For this reason only, the skilled person would not revert to Ikeda.

Suspensions are mentioned in a list of possible dosage forms. *See* Ikeda at col. 13, lines 51-58. The process for manufacturing liquid dosage forms is stated at column 14, lines 37-39, referring back to the method of manufacturing injections. Injections are identified at column 14, lines 12-28. Again, no preference or emphasis is placed on suspensions. From a reading of Ikeda, the skilled person would not gain any specific knowledge about suspensions, let alone suspensions of the fibrate class of drugs, let alone suspensions of fenofibrate (which is one of fifteen fibrates identified by Ikeda), even less so of suspensions of micronized fenofibrate.

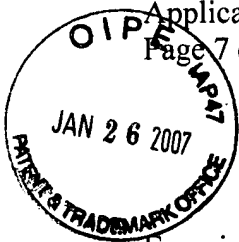
Thus, the skilled person would not contemplate reading Curtet and Ikeda together because they are concerned with two remote fields. More particularly, Ikeda is non-analogous art. There is nothing in Ikeda remotely related to the claimed invention.

As presented above, the claimed suspensions are not the dosage form to be administered to a patient, but an intermediate product used in the manufacture of a final dosage form with enhanced properties. Neither Curtet nor Ikeda discloses or suggests the use of suspensions as intermediate products in the manufacture of final dosage forms.

In view thereof, Applicants respectfully submit that the presently claimed invention is unobvious over Curtet in view of Ikeda, and respectfully request that the rejection under 35 USC § 103 be withdrawn.

⁵ Ikeda at column 11, line 1.

⁶ Ikeda at column 12, lines 1-5.



Information Disclosure Statements Filed in 2006

In the PTO-1449 Form returned to Applicants in conjunction with the Office Action, the Examiner indicated that she did not consider the following because they did not have a date:

- (i) Laboratoires Fournier undated document entitled "Fenofibrate Tablets 54-160 mg Dissolution Test Conditions Development Studies, Dissolution Test Specification Recommendations" (Filed May 8, 2006)
- (ii) Laboratoires Fournier's Lab Notebook Nos. 1 and 2 attached to the Bloquin Declaration. (Filed May 8, 2006)
- (iii) Laboratoires S.M.B. S.A. Report pages 1-4 (Filed June 19, 2006).

Applicants respectfully submit that the rules regarding the submission of materials to the PTO under 35 U.S.C., 37 C.F.R. and the MPEP do not require that the document have a date in order to be considered by the PTO. Applicants respectfully request that the Examiner consider these references or provide evidence from the USC, CFR or MPEP that undated documents must not be considered by the PTO.

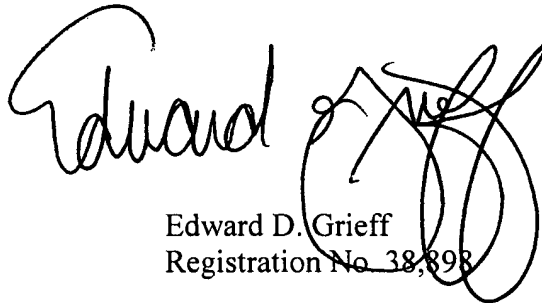
Additionally, the Examiner has considered the identical references in issued parent patents and related co-pending applications. It is unclear why the Examiner has considered these references in some applications and not in this application.

For the Examiner's convenience, Applicants are attaching hereto a PTO-1449 Form identifying these references so that they can be considered. Applicants respectfully request that the Examiner-initialed PTO-1449 Form be returned with the next PTO communication.

Conclusion

An early and favorable reconsideration and allowance of claims 1-61 is respectfully requested. Examiner Sheikh is encouraged to contact the undersigned to expedite prosecution of this application.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Edward D. Grieff', with a large, stylized circular flourish at the end.

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